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Correlation of Platelet Count with Grading of Esophageal Varices in Cirrhotic Patients

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Abstract

Background/Aims: Cirrhosis represents a late stage of progressive hepatic fibrosis and is generally considered to be irreversible in its advanced stages. Esophageal varix is a complication of liver cirrhosis and is the consequence of portal hypertension. The aim of this study was to determine the correlation between the severity of thrombocytopenia and the presenting of esophageal varices (EVs) in cirrhotic patient. **Patients and Methods:** This study was a retrospective, descriptive, analytic and monocentric study, which was carried out at Gastroenterology Department, Khmer Soviet Friendship Hospital, Phnom Penh, Cambodia. It was conducted from 1st September 2020 to 31st January 2021. All patients were diagnosed as liver cirrhosis by clinic, biology and ultrasound. Patients' data were noted in standardized questionnaire with information such as age, sex, address, laboratory result, and the result of endoscopic finding. All data were registered into a data set and then analyzed by SPSS program version 23. **Results:** 1445 patients were enrolled for gastroscopy. Only 303 patients (21%) were suggested for variceal screening after the exclusions. Male was predominant with sex ratio F/M (1/2.03). Patients' age varied between 21 and 80 years old, with the mean age of 55 ± 11 years old. 199 patients (66%) were found with EVs, while EVs grade 1 and 2 without red signs were predominated, accounting to 22.8% and 19.5% respectively. The majority of the patients with platelet count between 50 - 99 giga/l had EVs vs platelet count > 150 giga/l had no EVs ($p < 0.0001$). The cut-off level of platelet with EVs was 123 giga/l with 75% sensitivity and 65% specificity and with large varices was 105 giga/l with 70% sensitivity and 63% specificity. **Conclusion:** Thrombocytopenia is a non-invasive parameter with high accuracy for the prediction of EVs in cirrhosis. The severity of thrombocytopenia increased as the grading of EVs increased. Thus, it can assist in triaging cirrhotic patients for endoscopy to identify EVs.

Keywords

Liver Cirrhosis, Portal Hypertension, Esophageal Varices, Thrombocytopenia, Esophagogastroduodenoscopy

1. Introduction

Portal hypertension is a common complication of liver cirrhosis that can lead to develop esophageal varices (EVs), which are abnormally dilated veins within the wall of the esophagus that may lead to hemorrhage [1]. The majority of patients with cirrhosis will develop EVs, and about a third of these patients will have at least one bleeding episode due to the rupture of a varix [2] [3]. Majority of cirrhotic patients present late with advance disease and most of them have large varices on their first screening [4]. For this reason, endoscopic screening to detect the EVs is part of the diagnostic work-up in cirrhotic patients. Furthermore, this screening is also for prophylactic treatment's purpose [5].

Upper gastrointestinal bleeding (UGIB) is the most common gastroenterological emergency. It refers to the bleeding originating from sites in the esophagus, stomach, or duodenum till the ligament of Treitz [6]. The two principal causes of UGIB are peptic ulcer disease (PUD) and bleeding related to the portal hypertension (UGIB-PHT) as variceal bleeding which accounts for 50% - 90% and 10% - 30% respectively [7]. UGIB-Variceal rupture is caused by a portal hypertension mostly in liver cirrhosis. In clinical practice, to manage the variceal bleeding precisely and promptly, administration of vasoactive drugs to these patients is important, because variceal bleeding has a very high early mortality rate of up to 30% [8]. However, giving vasoactive agents to every patient is very cost-effective especially in the developing country. Therefore, all physicians should be capable to distinguish which patients the bleeding is in favor from varices and those whose is not in favor from varices based on the initial physical examination and the result of basic laboratory parameters. For these reasons, endoscopic screening to detect the presence of EVs is part of the diagnostic work-up in patients with cirrhosis, and to identify which patient is urgently needed for prophylactic treatment or not [5].

Recently, AASLD practice guidelines stated that the screening esophagogastroduodenoscopy (EGD) for the diagnosis of esophageal and gastric varices is recommended when the diagnosis of cirrhosis is made [5]. However, this is a rather unpleasant method that carries a certain risk of complications and some time with no benefit for the patients themselves [9].

Thrombocytopenia (platelet count < 150,000/μL) is a common complication in patients with chronic liver disease (CLD) [10]. It is reported in as many as 76% of cirrhotic patients [11]. The exact pathogenesis of this thrombocytopenia is multifactorial which include with decrease the production of thrombopoietin, the result of splenic sequestration of platelets, and the myelosuppression of platelet production due to hepatitis C virus (HCV) [12]. Endoscopic screening is

usually recommended for early detection of EVs in cirrhotic patients with portal hypertension. Unfortunately, this approach is limited by its invasiveness and cost [13]. Thus, we decided to formulate this retrospective study of Cambodian patients with liver cirrhosis to determine whether the platelet count can predict the presence and/or the size of EVs, while the presenting of medium and large-sized varices is the essential indication for prophylactic therapy especially with esophageal band ligation. The aim of this study was to assess the possibility of utilizing the platelet count whether it can spare the patients at low risk for variceal bleeding from endoscopic screening.

2. Patients and Methods

2.1. Study Design

This is a retrospective, descriptive, analytical, and single center study.

2.2. Study Setting

This study was conducted from 1st August 2020 to 31st January 2021, at Gastroenterology Department of Khmer Soviet Friendship Hospital, Phnom Penh, Cambodia.

2.3. Study Population

344 cases were eligible to be included in this study from the existing database of 1446 patients admitted at Gastrointestinal Department of Khmer Soviet Friendship Hospital who were performed endoscopy for vary indications. Patient's data was well documented in a standardized questionnaire.

2.4. Sample and Sampling Methods

344 patients estimated to be included in this study. Patients' data were noted in standardized questionnaire with information such as age, sex, laboratory result, and the result of basis endoscopic finding.

Inclusion criteria

Ether gender and all cirrhotic patients with age ≥ 18 years old.

Exclusion criteria

Incomplete data (laboratory and/or endoscopic result), patient with history of esophageal variceal band ligation, variceal upper gastrointestinal bleeding and HCC or hepatic tumors.

2.5. Data Collection Instrument

All our study equipment, we used the clinical and paraclinical records, the registered notebooks of cirrhotic patients retrospectively using a questionnaire form.

2.6. Data Collection

Data were collected by a physician, the author of this study, supervised and verified clinically by experienced doctors at the time of the patients' presentation in-

cluded age, gender. Initial laboratory data included hemoglobin, white blood cell count, platelet count, albumin, creatinine, prothrombin time and bilirubin.

2.7. Data Entry and Analysis

Statistical analysis was performed using the SPSS software, version 23. The level of statistical significance was set at $p < 0.05$. The prediction value of the platelet was assessed by using the area under the ROC (AUROC). The cutoff value was chosen where sensitivity and specificity were maximal. We calculated the sensitivity, specificity to find the threshold value of platelet.

2.8. Ethical Consideration

All collections of data were made only after agreement in Khmer-Soviet Friendship Hospital and University of Health Sciences, Phnom Penh, Cambodia. The patient's identifications are not shown.

3. Results

3.1. Basic of Participation of the Study Population

The total patients who enrolled at Gastroenterology Department at Khmer Soviet Friendship Hospital for gastroscopy during the study period were 1446. Amount those patients, 1102 patients were suggested for other reason beside of variceal screening, and 41 patients were excluded in patients with HCC, liver tumors and incomplete files. Finally, we had only 303 (21%) patients been included in our study for variceal screening in cirrhotic patients (Figure 1).

We found the total of the women were 100 (33%) and males were 203 (67%) with sex ratio (F/M) of 1:2.03.

The patients were aged from 21 years to 80 years. The mean age of those patients were 55 ± 11 years old. We also grouped the age into 10 years' intervals. Figure 2 illustrated the 6 groups of age, we found one patient starting from 19 - 29 years old (0.3%), 28 patients from 30 - 39 years old (9.2%), 57 patients from 40 - 49 years old (18.8%), 98 patients from 50 - 59 years old (32.3%), 82 patients from 60 - 69 years old (27.1%) and 37 patients at the age ≥ 70 years (12.3%). We noted the group age of 50 to 69 years old, the patients were frequent suggested for gastroscopy to detect the EVs if compare to the other age groups.

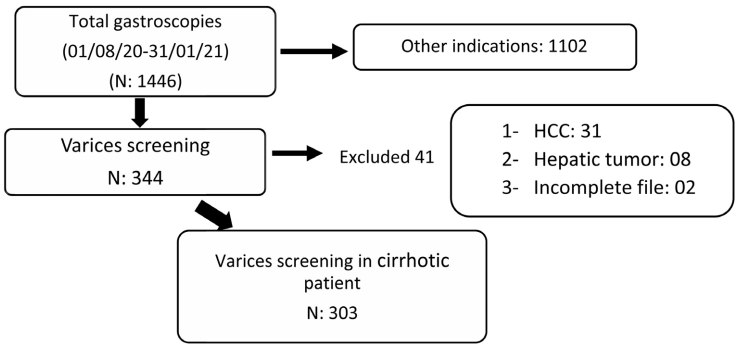

Figure 1. Flow chart of our study population.

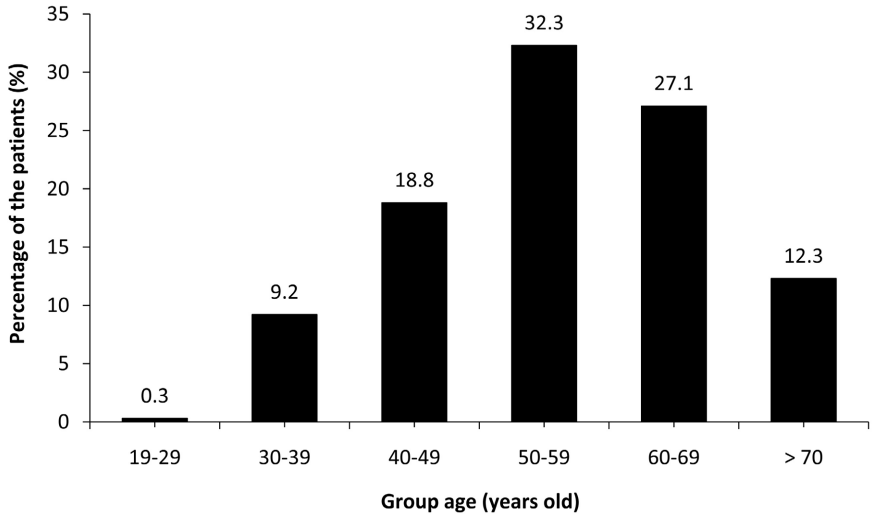

Figure 2. Frequency of age group.

3.2. General Characteristics of the Analyzed Study Population

The patients who enrolled had platelet level from 16 giga/l to 677 giga/l. The mean platelet of those patients was 163 ± 107 giga/l. To facilitate the comparison of the platelet count with the frequency of EVs, we devised the platelet count into the group of 50 giga/l intervals. **Figure 3** illustrated that 4 groups of platelet count were classified. Twenty patients in group starting from 16 - 49 giga/l (6.6%), 80 patients in group 50 - 99 giga/l (26.4%), 67 patients in group 100 - 149 giga/l (22.1%), and 136 patients in group ≥ 150 giga/l (44.9%) were found. In this platelet group, most of the patients with cirrhosis who were asked for variceal screening was in the platelet group > 150 giga/l.

303 cases (21%) were enrolled for variceal finding in cirrhotic patients. Hundred-ninety-nine patients (66%) were found the esophageal varices. Based on the endoscopic grading, the incidence of grade 2 EVs without red signs and grade 1 esophageal varices were predominated, accounting to 59 cases (19.5%) and 69 cases (22.8%) respectively. However, esophageal varices grade 2 with red signs were 19 cases (6.3%), grade 3 were 52 cases (17.2%) and varices were absence in 104 cases (34.2%) (**Figure 4**).

The statistical analysis showed that males had acquired more frequent than females in terms of EVs and also in the absence of EVs. The statistical analysis using Chi-square test showed there was no significant different between both genders and the presence of EVs ($p = 0.99$) (**Table 1**).

This statistical analysis demonstrated that 73 (24.1%) patients of all population in this study had large EVs (EVs grade II with red signs and grade III), while 230 (75.9%) patients had small EVs (EVs grade I and grade II without red signs) or absence of EVs (**Table 2**).

3.3. Correlation of Platelet Group and Grading of EVs

According to this statistical analysis demonstrated that out of 20 patients (6.6%)

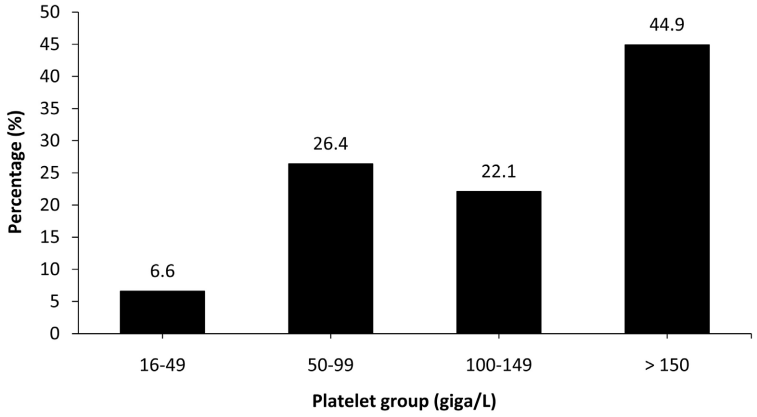

Figure 3. Distribution according to the platelet group.

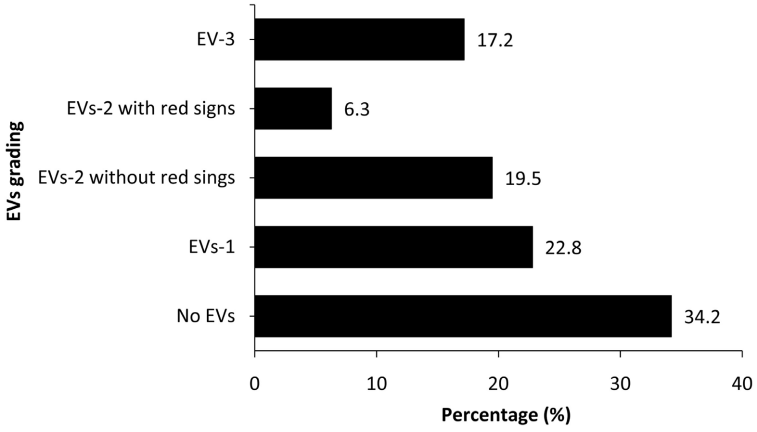

Figure 4. Distribution according to EVs grading.

Table 1. Frequency of EVs grading among the gender.

	Esophageal varices (EVs)						
Sex	**No EVs**	**EVs I**	**EVs II – RS**	**EVs II + RS**	**EVs III**	**Total (%)**	**p-Value***
Male (%)	69 (22.8)	46 (15.2)	39 (12.9)	13 (4.3)	36 (11.9)	203 (67.0)	0.99
Female (%)	35 (11.6)	23 (7.6)	20 (6.6)	6 (2.0)	16 (5.3)	100 (33.3)	
Total (%)	104 (34.3)	69 (22.8)	59 (19.5)	19 (6.3)	52 (17.2)	303 (100)	

*p Value for Pearson's X^2 or Fisher's exact test (and ANOVA) was used for comparison of categorical data between different grade of EVs with the sex of the patients.

Table 2. Distribution according to the presence of large EVs.

Large EVs	No. of patients	Percent (%)
Yes	73	24.1
No	230	75.9
Total	303	100.0

in platelet count between 16 - 49 giga/l, we found that 5 (25%) patients had EVs grade 3, 5 (25%) patients had EVs grade 2 with red signs, 2 (10%) patients had EVs grade 1 and 2 (10%) has EVs grade 2 without red signs. Out of 80 (26.4%) patients in platelet count between 50 - 99 giga/l, 19 (23.8%) patients had EVs grade 3, 8 (10%) patients had EVs grade 2 with red signs, 24 (30%) patients had EVs grade 2 without red signs and 19 (23.8%) had EVs grade I were noted. Out of 67 patients (22.1%) in platelet count between 100 - 149 giga/l, it showed us that 14 (20.9%) patients had EVs grade 3, 5 (7.5%) patients had EVs grade 2 with red signs, 13 (19.4%) patients had EVs grade 2 without red signs and 18 (26.9%) had EVs grade I. Hundred-thirty-six patients in platelet count ≥ 150 giga/l (44.9%), 14 (10.3%), 1 (0.7%), 20 (14.7%), 30 (22.1%) patients had EVs grade III, II with red signs, grade II without reds signs and grade I respectively; and 71 (52.2%) patients had no EVs were found (Table 3).

From the correlation below, it is evident that majority of the patients having platelet count between 50 - 99 giga/l till 100 - 149 giga/l had esophageal varices, and patients having platelet count > 150 giga/l had no EVs ($p < 0.0001$).

Figure 5 demonstrated that the area under the curve (AUC) was 0.732 (95% confidence interval (CI): Lower bound = 0.670, upper bound = 0.795). ROC curve showed a close to 75% sensitivity and a close to 65% specificity of platelets count for the presence of EVs in cirrhotic patients at a cutoff value of 135 giga/l.

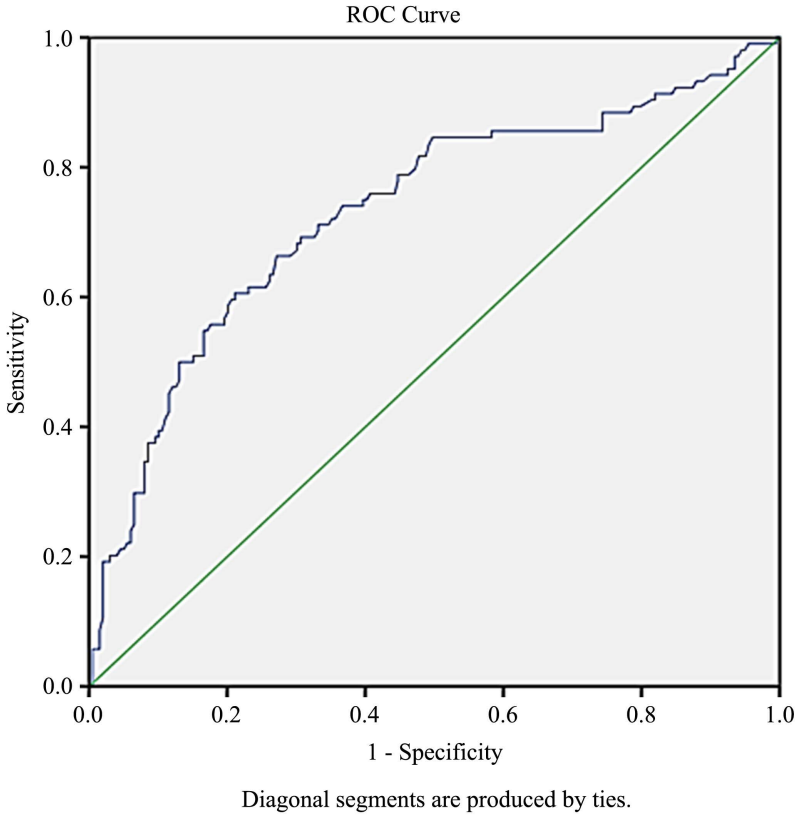

Figure 5. The graphical way of the connection/trade-off between sensitivity and specificity for possible platelets cut-off value for the presence of EVs in cirrhotic patients.

Table 3. Correlation of platelet group and EVs grading.

Platelet group (giga/l) (%)	Esophageal varices (EVs)						p-Value*
	No EVs	EVs I	EVs II − RS	EVs II + RS	EVs III	Total (%)	
16 - 49	6 (30.0)	2 (10.0)	2 (10.0)	5 (25.0)	5 (25.0)	20 (6.6)	<0.0001
50 - 99	10 (12.5)	19 (23.8)	24 (30.0)	8 (10.0)	19 (23.8)	80 (26.4)	
100 - 149	17 (25.4)	18 (26.9)	13 (19.4)	5 (7.5)	14 (20.9)	67 (22.1)	
150 - 677	71 (52.2)	30 (22.1)	20 (14.7)	1 (0.7)	14 (10.3)	136 (44.9)	
Total (%)	104 (34.3)	69 (22.8)	59 (19.5)	19 (6.3)	52 (17.2)	303 (100)	

*p Value for Pearson's X^2 or Fisher's exact test (and ANOVA) was used for comparison of categorical data between different grade of EVs with the group of platelets.

3.4. Correlation of Platelet Group and the Presence of Large EVs

When we observed in this statistical analysis, most of the patients in the study population in platelet group of 16 - 49 giga/l to platelet group 100 - 149 giga/l were found large EVs (p-value < 0.001). Furthermore, we found less patients with platelet ≥ 150 giga/l had large EVs, only 16 cases (21.9%) vs 120 cases (52.2%) with no large EVs (p < 0.0001) (Table 4).

Figure 6 demonstrated that AUC was 0.698 (95% CI: Lower bound = 0.631, upper bound = 0.765). ROC curve showed a close to 70% sensitivity and a close to 63% specificity of platelets count for the presence of large EVs in cirrhotic patients at a cutoff value of 105 giga/l.

In this statistical analyzing, we also tried to set the value of platelet below 150 giga//L to determine the presenting of EVs as in the theory showed that the platelet counts under those value had the risk of EVs presenting in cirrhotic patient (BAVENO VI) [14]. As the result, 57 patients (78.1%) had EVs with platelet count < 150 giga/L vs 16 cases (21.9%) with platelet counts > 150 giga/L (Table 5).

4. Discussion

UGIB is a fetal complication of portal hypertension, develops in about 30% - 40% of the patients with cirrhosis due to the severity of chronic liver disease. Variceal hemorrhage is associated with significant morbidity, mortality and health care costs. Numerous studies have demonstrated the efficacy of beta blockers for the primary prevention of variceal bleeding in patients with high-risk, indicating the gastroscopy for screening the esophageal varices. Current guidelines recommend that all cirrhosis patients should undergo endoscopic screening at the time of diagnosis of cirrhosis to identify those at high risk of

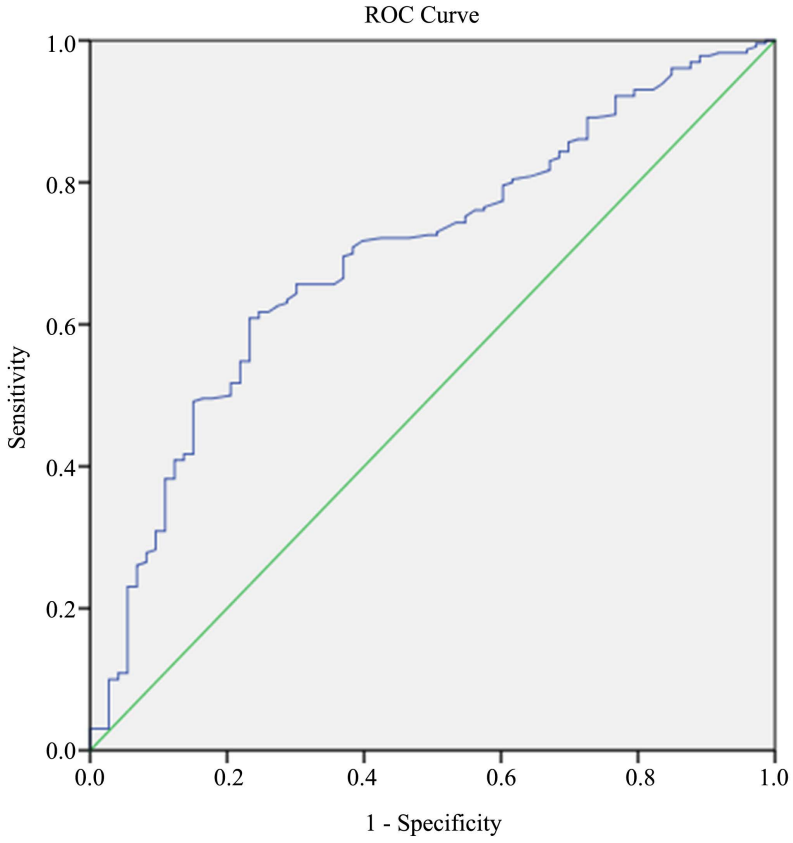

Figure 6. The graphical way of the connection/trade-off between sensitivity and specificity for possible platelets cut-off value in patients with large EVs.

Table 4. Correlation of platelet group and large EVs.

	Large esophageal varices (EVs)				
Platelet group (giga/L)	**Yes (n = 73, 24.1%)**		**No (n = 230, 75.9%)**		**p-Value***
16 - 49	10	13.7%	10	4.3%	<0.001
50 - 99	27	37%	53	23.0%	
100 - 149	20	27.4%	47	20.4%	
150 - 667	16	21.9%	120	52.2%	

*p Value for Pearson's X^2 or Fisher's exact test (and ANOVA) was used for comparison of categorical data between large and non-large EVs with the group of platelets.

Table 5. Correlation of platelet group (> vs <150 giga/L) and large EVs.

	Large EVs				
Platelet group	**Yes (n = 73, 24.1%)**		**No (n = 230, 75.9%)**		**p-Value**
<150 giga/L	57	78.1%	111	48.3%	<0.001
>150 giga/L	16	21.9%	119	51.7%	

*p Value for Pearson's X^2 or Fisher's exact test (and ANOVA) was used for comparison of categorical data between large and non-large EVs with platelet count.

bleeding and likely to benefit from primary prophylaxis. This approach, however, places a heavy burden on endoscopy units and the repeated testing over time can decrease patient compliance.

However, there is a particular need for non-invasive predictors for the presence EVs to ease the medical social and economic burden of the disease. Interestedly, according to the many previous studies have shown a good predictive value of different non endoscopic variables for the presence or absence of gastro-esophageal varices. Platelet value with or without the size of the spleen was one of those non endoscopic variables for the prediction the presenting of esophageal varices in many studies.

This study revealed a very similar result in sex distribution with many studies done in various countries. Three-fifths of our patients were male, providing a male predominance with the sex ratio M/F = 2.03/1. Based on other studies, for example, Duah A, *et al.* in 2018 took place in Africa demonstrated that men had suffered from liver cirrhosis more than women with sex ratio of M/F = 3.5/1 [4]. Furthermore, the study of Chang PE, *et al.* in 2015 in Singapore disclosed the result of sex ratio M/F = 1.76/1 but non-significant difference [15]. The study of Topdagi O, *et al.* in 2014 took place in Turkey illustrated the men had suffered from liver cirrhosis more than women with the sex ratio M/F = 1.38/1 [16]. Recently study in 2019, conducted in Pakistan by Lohana RK, *et al.* showed that liver cirrhosis was also predominant in men with the sex ratio M/F = 2.6/1 [17]. Likewise, we found similarly with the local study of KHY, M. in 2021 at Calmette's hospital in Cambodia. His study revealed the sex ratio M/F = 1.5/1 [18].

Therefore, this male predominance in liver cirrhosis might be related to the higher degree involvement to risk factors in men than in women. Alcohol intake, which is one of the most common causes of cirrhosis, is heavier in men than in women [19] [20]. Higher prevalence of chronic hepatitis B and C in men than in women is another possible explanation of this male predominance. According to Khan F, *et al.* chronic hepatitis B and C are more common in men than in women [21] [22].

In this study, the age of patients varies between 21 and 80 years old. The mean age of patients with liver cirrhosis regardless of its etiology or the presence of EVs was about 55 with the standard deviation of 11 (mean age: 55 ± 11). There were 6 age-groups in this study but the most represented group is between 50 and 69 years old. Indeed, the study carried out in Singapore by Chang PE, *et al.* in 2015 showed that the average age of patients with liver cirrhosis was 61 years old [15], while around 60 years old in Italy according to the study of Stroffolini T, *et al.* which carried out in 2017 [23]. A study conducted by Amouretti M, *et al.* which took place in France in 2000 found that the mean age of patients with liver cirrhosis was 65 years old [24]. Based on our result, the age was younger in our patients as compare to the developed countries/Western countries. On the other hand, the study carried out in Turkey by Topdagi O, *et al.* in 2014 showed that the average of patients with liver cirrhosis was 55 years old [16], while around 46 years old in Pakistan according to the study of Lohana RK, *et al.* in

2019 [17]. In 2018, according to the study of Duah A, *et al.* in Africa, proved that the mean age was 45 years old [4]. Recently study in India by Priyadarshi BP, *et al.* in 2020 demonstrated that the mean age of patients with liver cirrhosis was 48 years old [25]. Another recent study in Cambodia conducted by Khy Makara in 2021 proved that the mean age of those patients was 59 years old which is very closely to our study [18].

These differences can be explained by the causes of liver disease in different countries. As we found, if we compare to the Westerners countries such as France and Italy, the Asian and African population who were diagnosed with liver cirrhosis was younger. This tendency of younger age can probably be linked to the early onset of viral transmission in our population. The study conducted by Lavanchy D. which first published on 20 February 2004 said that in Western countries, the disease is relatively rare and acquired primarily in adulthood, whereas in Asia and most of Africa, chronic HBV infection is common and usually acquired perinatally or in childhood [26].

As a result, the onset of cirrhosis in our patients was in younger age as compare to those in Western patients. On the other hand, in industrialized countries such as France and Italy, alcohol is the most common cause of liver cirrhosis and alcohol consumption habits are in adulthood [27]. That's why they found the average age of patients who had liver disease were older than us.

Those 199 patients, who had EVs, were found in the group platelet count between 50 - 99 giga/l. It was evident that 70 patients (32.5%) had EVs. Controversially, in group platelet count > 150 giga/l, 70% was found no EVs were found highly significant (p-value < 0.0001). Grading of esophageal varices was inversely correlated with platelet count in our study. This finding is similar to the study in Pakistan by Abbasi A, *et al.* in 2010 [11] which stated that the severity of thrombocytopenia increased as the grading of esophageal varices increased.

Another study that was conducted by Nouh MA, *et al.* in Egypt in 2018 [28] stated that the platelet count was statistically significantly lower in patients with EVs grades I, II, and III (100.5 ± 19.8, 65.2 ± 13.0, and 60.3 ± 14.1 × 10^3/mm^3, respectively) than in those without EVs (152.1 ± 17.1 × 10^3/mm^3). There was a highly significant negative correlation between platelet count and esophageal variceal grading ($r = -0.756$; $p < 0.001$) [28]. This result is the same as our present study.

Further study in India by Priyadarshi BP, *et al.* in 2020 [25] also illustrated that 44 patients had their platelet count less than 100 giga/l. Twenty-four patients were found grade 2 varices followed by 14 patients with grade 3 varices with p-value highly significant ($p < 0.001$). This study finding was similar to our present study proved that the severity of thrombocytopenia increased the severity of esophageal varices.

Recent local study of Khy Makara at Calmette hospital [18], showed that it is evident that all 101 (100%) patients with the platelet count between 50 - 99 giga/l had esophageal varices, while 45 (54.9%) patients had no EVs with the platelet count > 150 giga/l ($p < 0.0001$). His finding was strongly positive with the low

platelet count group (group platelet 50 - 99 giga/l) while ours found only 87.5% of patients in those group had EVs vs 52.2% had no EVs in group platelet > 150 giga/l. However, in both studies had the same conclusion which showed that EVs were mostly found in platelet group of 50 - 99 giga/l and less found when the platelet > 150 giga/l.

This study showed that the severity of thrombocytopenia increased as the grading of esophageal varices increased. Moreover, on this statistical analysis study proved that 135 giga/l of platelet count was the cut-off value for the presence of EVs with 75% sensitivity and 65% specificity. This result is similar to the study which is conducted by Nouh MA, *et al.* in Egypt in 2018 [28] which illustrated that the cut-off value of platelet count as a predictor for the presence of varices was less than or equal to 130 giga/l with a sensitivity of 95% and specificity of 95%.

Many others studies were conducted to evaluate the role of platelet count as a predictor of the presence of varices. One study in Pakistan conducted in 2004 by Gill M, *et al.* [29] which studied on 140 patients with chronic liver disease. They concluded that the platelet count of 100 giga/l is a reliable marker for predicting EVs in cirrhotic patients. Another study in India by Rani KV, *et al.* in 2015 [30], the platelet count less than 140 giga/l was considered as a noninvasive predictor of EVs.

These different studies above could be explained by the different populations studied as regards the etiology of cirrhosis and/or the stage of the disease [31]. For example, the cut-off value of platelet count in our population study was higher than those in Egypt and Pakistan maybe due to the late stage of disease in most of the patients who admitted in hospital during the study period.

However, it's similar to the local study of Khy Makara at Calmette hospital during 2016 to 2017 with the cut-off value of 125 giga/l [18]. This similar finding can be explained by same local study.

In this study, the cut-off value of platelet count as a predictor for the presence of large EVs was 105 giga/l with 70% sensitivity and 63% specificity. This result is very similar to the study which was conducted by Nouh MA, *et al.* in Egypt in 2018 [28] demonstrated that the cut-off value of platelet count as a predictor for the presence of large varices was less than or equal to 80 giga/l with a sensitivity of 91.2%, a specificity of 86.7%, positive predictive value of 90.1% and negative predictive value of 88.1%.

Sarwar S, *et al.* [32] in Pakistan in 2005 which 101 patients were included. They reported that patients with platelet count less than 88 giga/l were more likely to be associated with high-grade varices. Furthermore, there was a study in India by Cherian JV, *et al.* [33] in 2011 which studied on 229 patients. They reported that platelet count less than 90 giga/l was significantly associated with the presence of large EVs.

The recent local study of Khy Makara at Calmette hospital [18], 82 giga/l of platelet count was concluded as the cut-off value for predicting the presence of large EVs in his population study.

However, the cut-off value as the predictor the presenting of large EVs was higher than others. This higher platelet count finding maybe because of our patients were diagnosed at the early age if compare to others (mean age = 55) their chronic liver disease. Thus, the severity of their disease is better than patients in other studies.

5. Limitations

Based on the result of our study, there are several limitations such as its small sample size, a retrospective study and in only a single center. Furthermore, it should be more accurate if we can combine with liver stiffness and also the size of spleen in cirrhotic patients to predict the grading of EVs more accuracy. Therefore, more studies will be needed to validate these results in order to find the best way to predict the grading of EVs in cirrhotic patients in our country.

6. Conclusions

According to this study, we found the majority of cirrhotic patients are male with the mean age of 55 ± 11 years old. Based on the cut-off value of platelet count with the presentation of EVs in cirrhotic patients, platelet count less than 135 giga/l is a predicting factor in which the EVs can be found with high sensitivity and specificity. Furthermore, platelet count less than 105 giga/l can be the cut-off value as a predictor for the presence of large EVs with high sensitivity and specificity.

The platelet count is a non-invasive parameter with high accuracy for the prediction of esophageal varices. In cirrhotic patients with normal platelet counts, especially in financially deprived developing countries, can be waiting for endoscopic screening while they are at low risk for the presence of esophageal varices and its bleeding. However, when the platelet count < 135 giga/l, the gastroscopy has high yield for diagnostic and therapeutic tool of esophageal varices.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

Author Contributions to Manuscript

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data of data for the work: UONG, CHEY, SOU.
- Drafting the article or revising it critically for important intellectual content: UONG, UNN, CHEY, NY, CHHIT, CHHAY, KHUON.
- Final approval of the version to be published: UONG, CHEY, UNN, NOV, KANG, UN, KAING, KHUON, NY, MON, KANN, CHHIT, UM, CHHAY, SOU

- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: UONG, CHEY, UNN, NOV, KANG, UN, KAING, KHUON, NY, MON, KANN, CHHIT, UM, CHHAY, SOU

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